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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,417	08/14/2002	Rainer H Muller	668-59190	8775

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EXAMINER	
EBRAHIM, NABILA G	

ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
07/09/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Office Action Summary	Application No.	Applicant(s)	
	10/030,417	MULLER ET AL.	
	Examiner	Art Unit	
	NABILA G. EBRAHIM	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,20,22-34 and 36-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18, 20, 22-34, and 36-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/28/08 has been entered.

Receipt of Applicant's remarks and amendments to the claims dated 02/28/2008 is acknowledged.

Status of Claims

Claims 1-18, 20, 22-34, and 36-47 are pending in the application.

Claims 19, 21 and 35 were cancelled.

Status of Office Action: Non-Final.

Claim Rejections - 35 USC § 102

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

In view of amending the claims, the rejection of claims 1-4, 7, 10, 11, 13, 15, 22 and 27 remain rejected under 35 USC I02(b) as anticipated by Muller et al US 5, 858, 410 (Muller). Muller teaches a method for preparing nanoparticles of drugs e.g., corticoids such as prednisolone (col. 22, lines 40-45), the drug particles having average size of 10-1,000 nanometers made by dispersing solid therapeutically active drugs in a solvent and subjecting the dispersion to high-pressure homogenization in a piston-gap homogenizer (abstract and col. 20, lines 23-30) at room temperature (i.e. under 90 degrees; col. 20, lines 35-40).

Claims 1-4, 7, 10, 11, 13, 15, 22 and 27 are anticipated by Muller's '410.

With regard to the amendments to the claims reciting "water-reduced dispersion medium containing less than 80 wt% of water", this does not distinguish the instant claims form the prior art because Muller teaches a method to make a drug carrier subjecting a solid therapeutically active compound dispersed in a solvent to high pressure homogenization in a piston-gap homogenizer to form particles having an average diameter of 40 nm to 100 nm wherein said active compound is insoluble, only sparingly soluble or moderately soluble in water, aqueous media and/or organic solvents (claim 38), note that the use of the preposition "or" means the exclusion of the aqueous media in the dispersion which is interpreted as a non-aqueous solvent and a percentage of 0% water and consequently, less than 80%.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-18, 20, 22-34, and 36-47 remain rejected under 35 U.S.C.103(a) as being unpatentable over Desai et al WO 98/14174 in (Desai) view of Muller US 5, 858, 410 (Muller).

Desai et al (Patent WO '174) discloses a process for preparation of microparticles or nanoparticles of water insoluble drugs; e.g. paclitaxel, an agent that is insoluble in water and uses polymers such as polylactides and polyglycolides. The drug is dissolved in an organic solvent (page 17, lines l 5-25), a protein such as albumin is added to stabilize the nanoparticles (page 17, lines 31-34) and the mixture is homogenized under high-pressure homogenization (page 18, lines 6-15 and page 51, lines 25). In disclosing a method for making a pharmaceutically acceptable formulation, Desai discusses sterile-filtration and how drug of particle size less than 200 nm is obtained (page 19, lines 1-16, page 10, lines 24 and page 20, and lines 30-35). The drug particles can be in crystalline or amorphous for (page 13, lines 5-10); details of how to make drug particles of size less than 200 nm are provided. Furthermore, Desai et al also disclose the effect the solvent used has on drug particle size (page 38, lines 5-20) and further discuss the advantage of making the composition in the form of albumin-paclitaxel combination-low toxicity.

Regarding the amendments to the claims, the dispersion which have water-reduced dispersion medium containing less than 80 wt% of water is disclosed in Example 4 wherein the taxol is dispersed in ethanol which is free of water i.e. 0% water.

Desai did not disclose the piston-gap homogenizer required in claims 44-47

Muller has been discussed hereinabove.

Therefore it would have been obvious to one of ordinary skill in the art to make paclitaxel or nanoparticles according to the methods disclosed by Desai and homogenize it in a piston-gap homogenizer because Muller teaches that it is evident that by conversion of the microparticles into nanoparticles by means of a high-energy process, to increase the surface tension to such an extent that as a result the saturation solubility increases greatly (col. 6, lines 19+). The person of ordinary skill would have expected success of having a method of preparing

nanopaticles of an insoluble or barely soluble active agent using a high pressure homogenizing process in a piston-gap homogenizer and containing less than 80% of water.

Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill at the time the invention was made.

Response to Arguments

2. Applicant's arguments filed 02/28/2008 have been fully considered but they are not persuasive.

Rejection under 35 U.S.C §102 (b)

Applicant argues that:

All of the pending claims require "an anhydrous or water-reduced dispersion medium containing less than 80 wt % of water" as the dispersion medium, which was originally recited in claim 35. In view of the differences between Muller 410 and the claimed invention, withdrawal of the Section 102 rejection is respectfully requested.

To respond: Muller's discloses exclusion of the aqueous media in the dispersion which is interpreted as a non-aqueous solvent and a percentage of 0% water and consequently, less than 80% (see claim 13). Further, Desai teaches in Example 4 that taxol is dispersed in ethanol, ethanol is free of water i.e. 0% water.

Rejection under 35 U.S.C §103

Applicant argues the homogenization process which is disclosed by Chen et al. however, the argument renders moot in view of dropping Chen from the obviousness rejection under 35 U.S.C §103.

Applicant argues also that:

Desai teaches away from the claimed invention. See page 18, lines 16- 19 of Desai, where Desai describes "[a]cceptable methods of homogenization include processes imparting

high shear and cavitation. It is well known in the art that piston-gap homogenizers are used under conditions to form cavitation when water is the dispersion medium. Thus, the combination of Chen and Desai teach to use conventional cavitation, even if a piston-gap homogenizer is used in the theoretical method of Chen and Desai, which is in a direction away from the claimed invention.

To respond: Muller is relied upon for the use of piston-gap homogenizer. The reference teaches that the process increases the saturation solubility greatly (col. 6, lines 19+). In addition, Chen is not a reference of record as it is not included in the current office action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NABILA G. EBRAHIM whose telephone number is (571)272-8151. The examiner can normally be reached on 8:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nabila G Ebrahim/ /Michael G. Hartley/

Examiner, Art Unit 1618

Supervisory Patent Examiner, Art Unit 1618